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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/026,914	12/27/2001	Birgit Linhart	0273-0006	6890

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EXAMINER	
HINES, JANA A	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 01/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/026,914	LINHART ET AL.5	
	Examiner	Art Unit	
	Ja-Na Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 October 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,9,13-15 and 20-26* is/are pending in the application.

4a) Of the above claim(s) *7,9,22-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,13-15,20,21 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Amendment Entry

1. The amendment filed October 4, 2004 has been entered. Claims 1 and 26 have been currently amended. Claims 8, 10-12 and 16-19 have been cancelled. Claims 7,9, and 22-25 have been withdrawn. Claims 1-6, 13-15, 20-21 and 26 are under consideration in this office action.

2. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Withdrawal of Rejections

3. The following rejection has been withdrawn in view of applicants' amendments and arguments:

> The rejection of claims 1-3 and 13-14 under 35 U.S.C. 102(b) as being anticipated by Vrtala et al., (1996. J. Allergy Clin. Immun. Vol. 97(3): 781-787).

Response to Arguments

4. The rejection of claims 13-14 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained. The rejection was on the grounds that the specification and claims lack sufficient written description of the polynucleotide encoding the hybrid polypeptide. Applicants' assert that the polynucleotide and polypeptide sequences for the timothy grass pollen allergens were available in the art. However the claims are not just drawn to the entire polynucleotide and polypeptide sequences. Rather the claims encompass fragments thereof wherein each fragment consists of at

least eight consecutive amino acids from the respective allergenic proteins. There is no description of the fragments of nucleic acids that must encode the hybrid polypeptide. The instant specification does not provide for a method for preparing a hybrid polypeptide comprising fragments of polynucleotide. The specification does not provide a teaching of the fragmented structure, showing that nucleic and amino acid fragments were isolated at the time the invention was made, thus there is no teaching of a preparation method.

Applicants' urged that one of ordinary skill in the art armed with the instant specification, would understand the sequences used in the present invention. However, the standard is not that one would understand the sequences used in the present invention. To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See, e.g., *Moba, B.V. v. Diamond Automation, Inc.*, 325 F.3d 1306, 1319, 66 USPQ2d 1429, 1438 (Fed. Cir. 2003); *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d at 1563, 19 USPQ2d at 1116. Applicants' have not even pointed to support for the fragments thereof wherein each fragment consists of at least eight consecutive amino acids from the respective allergenic proteins. Thus no preparation method has been disclosed. Rather applicants' have disclosed the entire sequences but have failed to disclose a method for preparing a hybrid polypeptide comprising fragments consisting of at least eight consecutive amino acids from the respective allergenic proteins.

Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing

identifying characteristics sufficient to show that the applicant was in possession of the claimed invention. See, e.g., *Pfaff v. Wells Elecs., Inc.*, 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406; *Amgen, Inc. v. Chugai Pharmaceutical*, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991). Applicants' have failed to show that they were in possession of such. Moreover, it is noted that functional limitations alone are not sufficient to satisfy the written description requirement.

There is no conception of a method for preparing a hybrid polypeptide comprising fragments thereof as claimed at the time of filing. Furthermore, applicants have not taught what fragments will encode polynucleotides which are capable of encoding the polypeptide. There is no teaching of a representative fragment polynucleotide encoding a fragment of a polypeptide. In view of applicants' failure to explain the essential details the rejection is maintained.

Thus, in the absence of sequence information as claimed applicants arguments, declaration and amendments are not persuasive.

5. The written description rejection of claims 1-6, 13-15, 20-21 and 26 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained. The claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a hybrid polypeptide comprising at least two different plant allergenic proteins or fragments thereof, wherein the plant allergenic proteins are selected from the group consisting of Phl p1, Phl p2, Phl p5 and Phl p6 and wherein each fragment consists of at least eight consecutive amino acids of the respective allergenic protein and said hybrid polypeptide induces an antibody response.

Applicants assert that by amending the claims to recite the function of inducing an antibody response the rejection should be withdrawn. However, the specification fails to teach how to define fragments thereof with respect to which eight consecutive amino acids must be comprised therein to acquire the appropriate fragments. Neither the claims nor the specification teach how to obtain such fragments thereof. There is no guidance as to what amino acids may or may not be included without causing a detrimental effect to the fragments thereof as claimed. The claims broadly recite fragments thereof, therefore any fragment is being claimed, and no specific location requirement for particular amino acids is recited. Thus, the resulting fragments thereof could result in a functional fragment not taught and enabled by the specification. There is no written description of which eight amino acids must be comprised in the claimed hybrid polypeptide. Applicants' amendment does not overcome this lack of written description.

Applicants assert that because they have provided a generic definition of fragments at pages 2-3 of the instant specification and because the entire sequence is known one of skill in the art would understand that they were in

possession. However, this argument is not persuasive. With the exception of specifically recited sequences the skilled artisan cannot envision the detailed structure of the fragments thereof, thus conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. An adequate description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The nucleic acid and amino acid fragment sequences themselves are required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

A lack of adequate written description issue arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process as is the case here. Applicants' specification point out fragments can exist, however there is no disclosure of even one representative fragment. Thus one of skill in the art could not immediately envision the claimed fragments. See, e.g., *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996) (a "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not "reasonably lead" those skilled in the art to any particular species); *In re Ruschig*, 379 F.2d 990, 995, 154 USPQ 118, 123 (CCPA 1967) ("If n-propylamine had been used in making the compound instead of n-butylamine, the compound of claim 13 would have resulted. Appellants submit to us, as they did to the board, an imaginary

specific example patterned on specific example 6 by which the above butyl compound is made so that we can see what a simple change would have resulted in a specific supporting disclosure being present in the present specification. The trouble is that there is no such disclosure, easy though it is to imagine it.") (emphasis in original); *Purdue Pharma L.P. v. Faulding Inc.*, 230 F.3d 1320, 1328, 56 USPQ2d 1481, 1487 (Fed. Cir. 2000) ("the specification does not clearly disclose to the skilled artisan that the inventors ... considered the ratio... to be part of their invention .... There is therefore no force to Purdue's argument that the written description requirement was satisfied because the disclosure revealed a broad invention from which the [later-filed] claims carved out a patentable portion". Similarly, it appears that the instant case sets forth undisclosed fragments and asserts that these undisclosed fragments have some functional limitations. However, there is no actual disclosure of the claimed fragments. Moreover, the functional limitations do not constitute a written description of every species in a genus because it would not "reasonably lead" those skilled in the art to any particular species.

Applicants assert that they have conveyed with clarity to those skilled in the art that they were possession of the invention. However, at best applicants have shown that they were in possession of the entire sequence of timothy grass allergens, but applicants have not shown that they were in possession of fragments capable of inducing an antibody response. There is no disclosure of a highly conserved and immunogenic region in the plant allergen. Therefore, the specification lacks adequate support for the claims. Furthermore, *In The*

Reagents of the University of California v. Eli Lilly (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of amino acids by only their functional activity, i.e., inducing an antibody response does not provide an adequate description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

Currently the instant claims lack an adequate description of the fragments thereof, thus the descriptions are insufficient to support the claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645. Therefore, the full breadth of the claims fails to meet the written description provision of 35 USC 112, first paragraph and the rejection are maintained.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any

person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-6, 13-15, 20-21 and 26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection

Neither the specification nor originally presented claims provides support for a hybrid polypeptide comprising at least two different plant allergenic proteins or fragments thereof, wherein the plant allergenic proteins are selected from the group consisting of Phl p1, Phl p2, Phl p5 and Phl p6 and wherein each fragment consists of at least eight consecutive amino acids of the respective allergenic protein and said hybrid polypeptide induces an antibody response.

Applicant did not point to support in the specification for a hybrid polypeptide comprising fragments thereof wherein each fragment consists of at least eight consecutive amino acids of the respective allergenic protein and said hybrid polypeptide induces an antibody response. Moreover, applicant failed to specifically point to the identity or provide structural characteristics of fragments thereof wherein each fragment consists of at least eight consecutive amino acids of the respective allergenic protein and said hybrid polypeptide induces an antibody response. Thus, there appears to be no teaching of fragments thereof wherein each fragment consists of at least eight consecutive amino acids of the

respective allergenic protein and said hybrid polypeptide induces an antibody response.

Applicant has pointed to pages 2-3, 8 and 16-17 of the instant specification and claims for support of the amendment which are drawn to the fragments thereof wherein each fragment consists of at least eight consecutive amino acids of the respective allergenic protein and said hybrid polypeptide induces an antibody response, however it appears that the entire specification appears to fail to recite support for the new fragments. There is no teaching of any isolated fragments. There is no teaching of any fragments being comprised within a hybrid polypeptide. There is no teaching of a hybrid polypeptide comprising such fragments as inducing an antibody response in any host. Therefore, it appears that there is no support in the specification. Therefore, applicants must specifically point to page and line number support for the identity of fragments thereof wherein each fragment consists of at least eight consecutive amino acids of the respective allergenic protein and said hybrid polypeptide induces an antibody response as recited by the newly added amendments. Therefore, the new claims incorporate new matter and are accordingly rejected.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to

> be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 1-3 and 13-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ball et al., (WO 95/34578) in view of Vrtala et al., (1996. J. Allergy Clin. Immun. Vol. 97(3): 781-787).

The amended claims are drawn to a hybrid polypeptide comprising at least two different plant allergenic proteins or fragments thereof, wherein the plant allergenic proteins are selected from the group consisting of Phl p1, Phl p2, Phl p5 and Phl p6 and wherein each fragment consists of at least eight consecutive amino acids of the respective allergenic protein and said hybrid polypeptide induces an antibody response.

Ball et al., teach the major grass pollen allergen Phl pl. The recombinant DNA molecule may contain a nucleotide sequence which codes for a polypeptide which would induce an antibody response (page 3 lines 20-25). The invention teaches a recombinant or synthetic protein or polypeptide comprising as an essential part Phl pl (page 3 lines 33-35). The protein or polypeptide may be fused to an additional polypeptide, such as any other polypeptide that can be expressed as a fusion protein in prokaryotic or eukaryotic cells (page 4 lines 1-4). The invention also includes a recombinant DNA expression vector or cloning system (page 3 lines 26-30). Ball et al., while teaching that the Phl pl can be part of a hybrid or fusion polypeptide does not specifically recite using another plant allergenic protein within the hybrid polypeptide.

Vrtala et al., teach grass pollen allergens belong to the potent elicitors of type I allergy (abstract). Vrtala et al., teach that DNA coding for three major timothy grass pollen allergens representing group I (Phl p1), group II (Phl p 2) and group V (Phl p 5) was known (page 781). There is no relevant immunologic similarity between Phl p 2 and Phl p 1(page 781). The methods section teaches the construction of the expression plasmids for Phl p 1, Phl p 2 and Phl p 5 (page 782). cDNA clones were transcribed by polymerase chain reaction to DNA fragments coding for the mature allergens (page 782). Phl p 1 and Phl p 2, both of which contained ATG start codon in front of the coding region of the mature protein and genes were then inserted as fragments (page 782). The plasmids were transfected into *E.coli* host cells. The expression of the recombinant allergens in *E.coli* was also taught wherein cells were cultured, expressed, purified and thereby recovered (page 782).

Therefore it would have been prima facie obvious at the time of applicants' invention to modify the hybrid polypeptide as taught by Ball et al., to include a different plant allergen as taught by Vrtala et al., since Ball et al., already teach the need to have a hybrid or fusion polypeptide. Ball et al., teach that plant allergenic proteins such as Phl pI are amenable to being comprised within fusion proteins and/or hybrid polypeptides and can be fused to any other polypeptide that can be expressed as a fusion protein in prokaryotic or eukaryotic cells, while Vrtala et al., teach polypeptides that can be expressed in prokaryotic or eukaryotic cells, thus no more than routine skill would have been required to create a hybrid polypeptide comprising at least to different plant allergens. Thus,

there is a reasonable expectation of success in using the PhI pI of Ball et al., and any other polypeptide such as the ones taught by Vrtala et al., when the prior art teaches that all of these plant allergens can be expressed as a fusion protein in prokaryotic or eukaryotic cells.

Conclusion

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-

272-0859. The examiner can normally be reached on Monday-Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ja-Na Hines
January 4, 2005

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